

with the second solution comprising the second polyionic material having charges opposite of the charges of the first polyionic material.

REMARKS

In response to the Office Action dated March 26, 2002, Applicant respectfully requests reconsideration and withdrawal of the objections and rejections set-forth in the Office Action in view of the above amendments and the following remarks.

Claims 14-16 have been cancelled. Claims 1, 2, and 4-11 have been amended. Claim 17 is added. These amendments do not contain new matter and are fully supported by the specification. After these amendments are entered, fourteen (14) claims (Claims 1-13 and 17) remain pending in this application through this Amendment.

Specification Objections

Specification has been amended to incorporate all formula and to correct informalities.

Claim Objections Under 35 USC 112

Claims 1, 7, 8, and 11 have been amended to overcome the 35 U.S.C. §112, second paragraph, objections set forth in the Office Action.

Rejections Under 35 USC 102(b)

Applicants believe that a brief description of the present invention as claimed will assist the prosecution. The present invention is related to a method for modifying the surface of an article, the method comprising first functionalizing the surface of the article simply by applying one or more layers of each of one or more polyionic materials onto the surface of the article and then grafting any desired compound to the functionalized surface of the article. The Applicants' invention is partly based on the discovery that a layer of a polyionic material can be easily and stably formed on a polymeric article without any covalent attachment. Unlike plasma treatments and other techniques known in the prior art, the Applicants' invention can provide a cost-effective method for making biomedical devices such as contact lenses.

Claims 1-2, 5-6, and 12-13 were rejected under 35 USC 102(b) as being anticipated by Nakagawa et al. (US Pat. 5,409,731). The rejection over these claims is respectfully traversed for the following reasons.

Nakagawa teaches a surface modification method totally different from the Applicants' invention. In Nakagawa's method, an amino group containing polymer is cross-linked to the surface of a contact lens with the help of a cross-linking agent. In contrast to Nakagawa's method, the polyelectrolytic tie layer is not covalently attached to the surface of an article in the Applicants' invention. Furthermore, Nakagawa does not disclose or suggest anything about using of polyionic materials to functionalize the surface of an article in a non-covalent attachment manner. Applicants submit that the claimed invention are not anticipated by Nakagawa, since the cited reference teaches a surface modification totally different from the present invention as currently claimed. Applicants respectfully request withdrawal of the 35 U.S.C. §102(b) rejection.

Claims 1-2, 5-6, and 12-13 were rejected under 35 USC 102(b) as being anticipated by Wilson (U.S. Pat. 6,050,980). The rejection over these claims is respectfully traversed for the following reasons.

Wilson teaches a surface modification method totally different from the Applicants' invention. Wilson discloses a method comprising first dipping a contact lens in a solution of a crosslinking agent (hexamethylene diisocyanate) to form a tie layer and then attaching a thrombo-resistant layer (col.,7, lines 3-8). The tie layer is covalently attached to the surface of the lens. In contrast, the polyelectrolytic tie layer is not covalently attached to the surface of an article in the Applicants' invention. In addition, the crosslinking agent is not a polyionic material as required in the Applicants invention. Furthermore, Wilson does not disclose or suggest anything about using of polyionic materials to functionalize the surface of an article in a non-covalent attachment manner. Applicants submit that the claimed invention are not anticipated by Nakagawa, since the cited reference teaches a surface modification totally different from the present invention as currently claimed. Applicants respectfully request withdrawal of the 35 U.S.C. §102(b) rejection.

Claims 1-3, 5-6, and 12-15 were rejected under 35 USC 102(b) as being anticipated by Takemura et al (U.S. Pat. 4,876,126). The rejection over these claims is respectfully traversed for the following reasons.

Takemura teaches a method for forming a lubricating surface coating layer on a medical instrument. The lubricating surface coating layer is formed by covalently attaching to the medical instrument a natural water-soluble polymer or synthetic water-soluble polymer, which can be a polyionic material, for example, polyamines, poly-electrolytes, polystyrene sulfonate (col. 5, lines 4-7). Takemura does not disclose or suggest anything about using of polyionic materials to functionalize the surface of an article in a non-covalent attachment manner. Takemura teaches that when water-soluble polymers (including polyionic materials) are covalently bonded with the

surface of a substrate a lubricating layer carried on the substrate can be obtained that is not soluble in water and offers a lasting lubricating surface. Takemura teaches away from the Applicants' invention. Applicants submit that the claimed invention are not anticipated by Takemura for the above-mentioned reasons and respectfully request withdrawal of the 35 U.S.C. §102(b) rejection.

Claims 1-4, 6, 12-13 and 15 were rejected under 35 USC 102(b) as being anticipated by Vanderlaan et al. (U.S. Pat. 6,087,415). The rejection over these claims is respectfully traversed for the following reasons.

Vanderlaan teaches that biomedical devices are coated with an antimicrobial and hydrophilic coating by using a coupling agent. In Vanderlaan's method, the biomedical devices should contain hydroxy groups, amino groups, or both on the surface. Vanderlaan teaches that if the surface material of a medical device to be coated does not contain the requisite functional groups, such groups may be incorporated into the surface material, for example, by addition of one or more functional group-containing monomers into the polymers used to form the surface (col. 2, lines 48-61). Such method for functionalizing the surface of a medical device requires polymerization (covalently attachment of monomers). Vanderlaan does not disclose or suggest anything about using of polyionic materials to functionalize the surface of an article in a non-covalent attachment manner. Therefore, Applicants submit that the claimed invention are not anticipated by Takemura and respectfully request withdrawal of the 35 U.S.C. §102(b) rejection.

Rejections Under 35 USC 103(a)

Claims 4 and 16 were rejected under 35 USC 103(a) as being unpatentable over Takemura et al. Claim 16 has been canceled, and this rejection is therefore moot with respect to this claim. The rejection over claim 4 is respectfully traversed, since, as stated above, Takemura does not disclose or suggest anything about using of polyionic materials to functionalize the surface of an article in a non-covalent attachment manner. Takemura would not teach, suggest or motivate one skilled in the art to arrive at the present invention. Applicants submit that a *prima facie* case of obviousness can not be established and request withdrawal of the 35 U.S.C. §103(a) rejection.

Claims 7-11 and 16 were rejected under 35 USC 103(a) as being unpatentable over Vanderlaan et al. Claim 16 has been canceled, and this rejection is therefore moot with respect to this claim. The rejection over claims 7-11 is respectfully traversed for the following reasons.

As discussed above, Vanderlaan does not disclose or suggest anything about using of polyionic materials to functionalize the surface of an article in a non-covalent attachment manner. Vanderlaan would not teach, suggest or motivate one skilled in the art to arrive at the present invention. Applicants submit that a *prima facie* case of obviousness can not be established and request withdrawal of the 35 U.S.C. §103(a) rejection.

CONCLUSION

For the foregoing reasons, Applicants submit that Claims 1-13 and 17 are patentable over the cited prior art. Applicant respectfully requests reconsideration and withdrawal of the claim objections and rejections set-forth in the Office Action and allowance of claims 1-13 and 17.

Should the Examiner believe that a discussion with Applicants' representative would further the prosecution of this application, the Examiner is respectfully invited to contact the undersigned.

Please address all correspondence to Thomas Hoxie, Novartis Corporation, Patent & Trademark Department, 564 Morris Ave., Summit, NJ 0790-1027. The Commissioner is hereby authorized to charge any other fees which may be required under 37 C.F.R. §§1.16 and 1.17, or credit any overpayment, to Deposit Account No. 19-0134.

Respectfully submitted,



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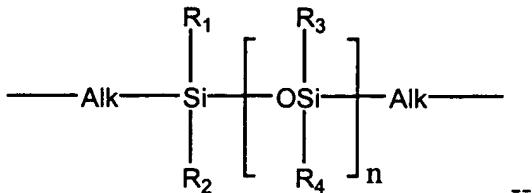
Date: June 26, 2002

Novartis Corporation
Patent and Trademark Department
564 Morris Avenue
Summit, NJ 07901

Version with Markings to Show Changes Made

In the Specification:

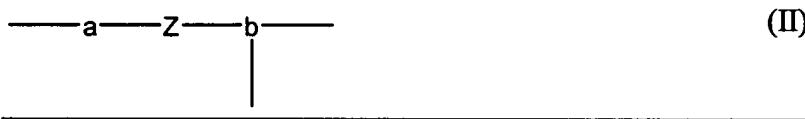
Page 12, immediately after heading (b) please insert –



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Page 14, please amend lines 4-15 as follows:

The polymers of this embodiment can be formed by polymerizing a macromer comprising at least one segment having the following general formula (II):

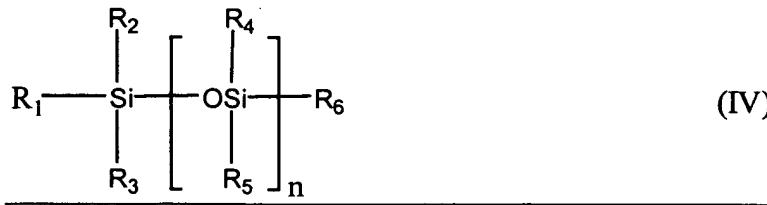


in which,

(a) is a polysiloxane segment,

Page 15, please amend lines 4-16 as follows:

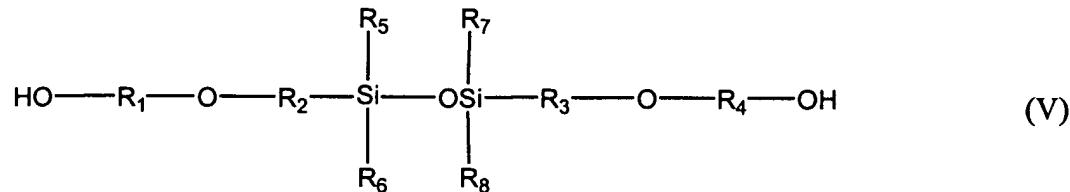
In one embodiment, a polysiloxane segment (a) can be derived from a compound having the following general formula (IV):



in which, n is an integer from 5 to 500;

Page 16, please amend lines 7-15 as follows:

Another embodiment of a substrate material of the present invention involves the polymerization of a siloxane-containing macromer formed from a poly(dialkylsiloxane) dialkoxyalkanol having the following structure (V):

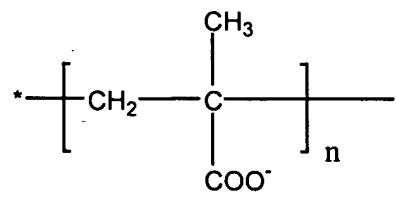


where n is an integer from about 5 to about 500, preferably about 20 to about 200, more preferably about 20 to about 100;

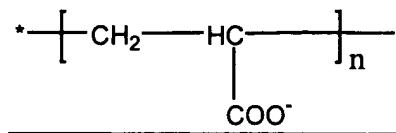
Page 21, please amend the whole page as follows:

meaning a []polyacrylic acid obtainable by []polymerizing acrylic acid in the []presence of suitable (minor) amounts of []a di- or polyvinyl compound.

Suitable []polyanionic material may be any material known in the art to have a plurality of negatively charged groups along a polymer chain. For example, suitable anionic materials can include, but are not limited to:
 (a) polymethacrylic acid (PMA)

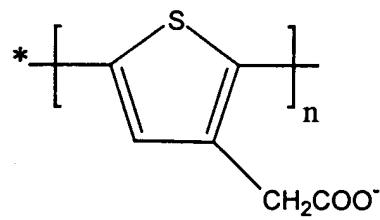


(b) polyacrylic acid (PAA)

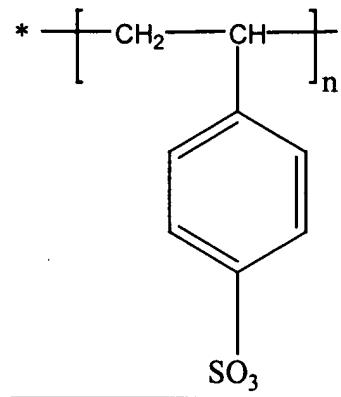


(c) poly(thiophene-[3-acetic acid) (PTAA)

Page 22, please amend the whole page as follow:



(d) poly(4-styrenesulfonic acid) (PSS) or sodium poly(styrene sulfonate) (SPS) or poly(sodium styrene sulfonate) (PSSS)



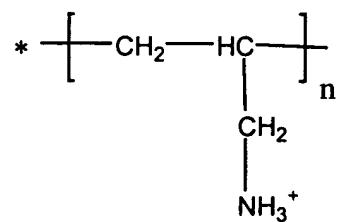
A suitable cationic substance may be any material known in the art to have a plurality of positively charged groups along a polymer chain. A cationic polymer may, for example, be a synthetic polymer, a biopolymer or modified biopolymer comprising primary,

secondary or tertiary amino groups or a suitable salt thereof, preferably an ophthalmically acceptable salt thereof when []ophthalmic devices are to be coated, for []example, a hydrohalogenide, []such as a hydrochloride thereof, in the []backbone or as substituents.

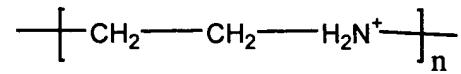
Various []cationic materials can include, but are not limited to:

(a) poly(allylamine hydrochloride) (PAH)

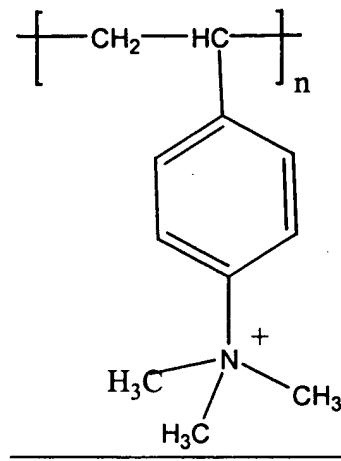
Page 23, please amend the whole page as follows:



[](b)
poly(ethyleneimine) (PEI)



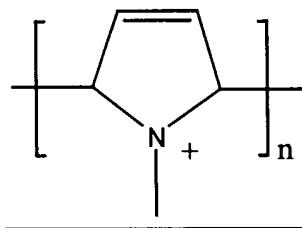
(c) poly(vinylbenzyltrimethylamine) (PVBT)



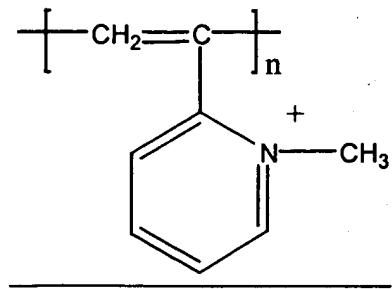
(d) polyaniline (PAN or PANI) (p-type doped) [or sulphonated polyaniline]

Page 24, please amend the whole page as follows:

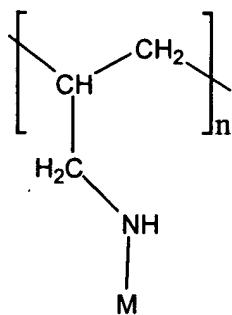
(e) polypyrrole (PPY) (p-[
]typed doped)



(f) poly(pyridinium [
]acetylene)



Page 25, on the top of the page please insert formula (1) as follows:



Page 28, after formula (6d) please insert formula (6e) –

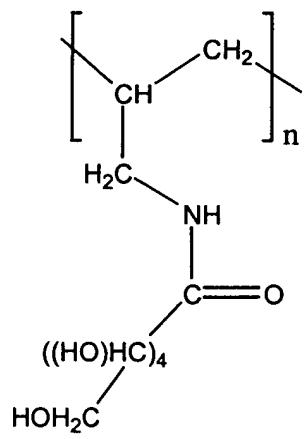


Page 29, please amend the whole page as follows:

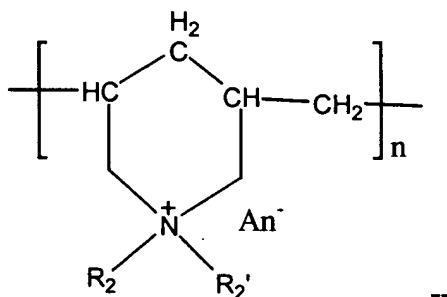
wherein X is halogen, preferably chlorine; (alk') is C₁-C₁₂-alkylene; R₁₂ is hydrogen or C₁-C₂-alkyl, preferably hydrogen or methyl; and R₃, R₄, R_{5'}, R₆ and Q₁ are as defined above. The reaction proceeds, for example, in an aqueous solution at room temperature or at an elevated temperature, such as from 25°C [] to about 60°C, and yields various [] polymers comprising various modifier [] units.

Because the [
amino groups of [
the compounds of [
proceeds, in [
the structure of the [
determined mainly [
the reactants that [
reaction. A particular polyionic material is polyallylamine gluconolactone,
as shown below in formula (7):

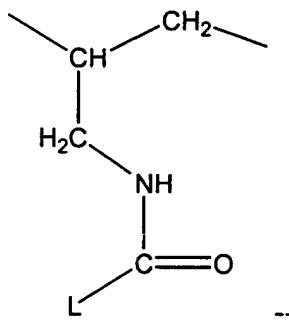
]reaction of the
]the polyallyl amine with
]formulae (6) or (6a)-(6k)
]general, quantitatively,
] modified polymers is
]by the stoichiometry of
]are employed into the



Page 30, after the last line please insert –

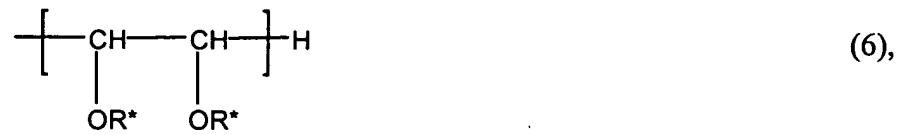


Page 32, before the first line please insert –



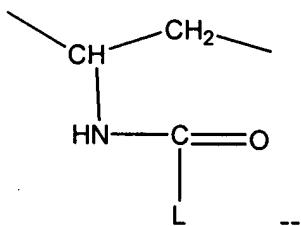
Page 32, please amend lines 9-21 as follows:

A particular embodiment relates to polyallyl amines comprising units of the above formula (5), wherein L is a radical of formula



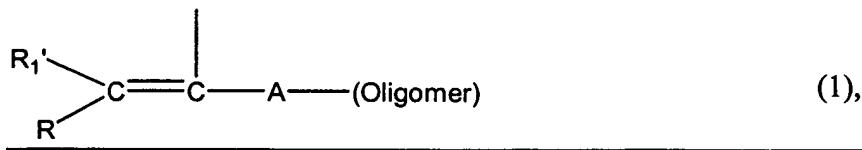
[
 (6),]
 wherein g is 1, 2, 3, 4 or 5, preferably 3 or 4 and in particular 4, each R* is independently hydrogen or a radical -C(O)-R29 or -C(O)-NH-R29', and for

Page 34, before the first line please insert –



Page 48, please amend the page as follows:

macromonomer such as, for example, a macromonomer having the formula



[(1),]

wherein R₁ is hydrogen, C₁-C₆-alkyl or a radical -COOR';

R, R' and R₁' are each independently of the other hydrogen or C₁-C₆-alkyl;

A is a direct bond or is a radical of formula

-C(O)-(A₁)_n-X- (2a) or

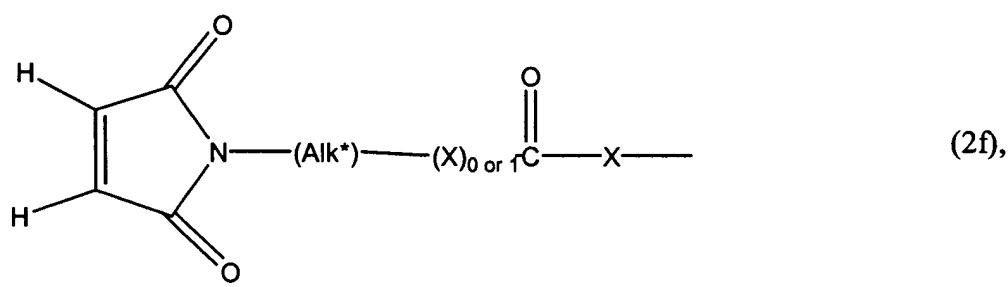
-(A₂)_m-NH-C(O)-X- (2b); or

-(A₂)_m-X-C(O)- (2c); or

-C(O)-NH-C(O)-X- (2d); or

-C(O)-X₁-(alk^{*})-X-C(O)- (2e); or

A and R₁, together with the adjacent double bond, are a radical of formula



[(2f),]

A₁ is -O-C₂-C₁₂-alkylene which is unsubstituted or substituted by hydroxy,

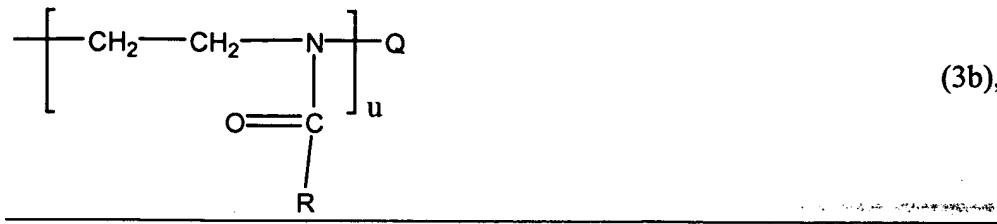
or is -O-C₂-C₁₂-alkylene-NH-C(O)- or -O-C₂-C₁₂-alkylene-O-C(O)-NH-R₁₁-

NH-C(O)-, wherein

R₁₁ is linear or branched C₁-C₁₈-alkylene or unsubstituted or C₁-C₄-alkyl- or C₁-C₄-alkoxy-substituted C₆-C₁₀-arylene, C₇-C₁₈-aralkylene, C₆-C₁₀-arylene-C₁-C₂-alkylene-C₆-C₁₀-arylene, C₃-C₈-cycloalkylene, C₃-C₈-cycloalkylene-C₁-C₆-alkylene, C₃-C₈-cycloalkylene-C₁-C₂-alkylene-

Page 50, please amend lines 21-22 as follows:

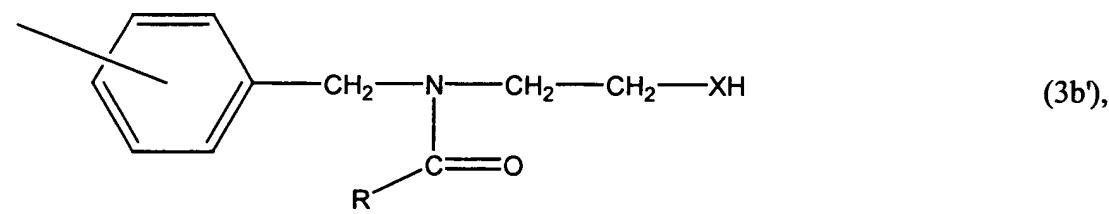
(ii) the radical of an oligomer of the formula



[(3b),]

Page 50, please amend lines 4-13 as follows:

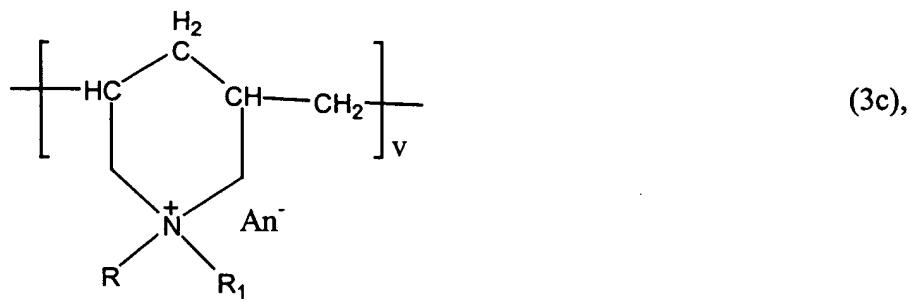
(iii) the radical of formula



[(3b')]

wherein R₂₈, X and u are as defined above, or

(iv) the radical of an oligomer of formula

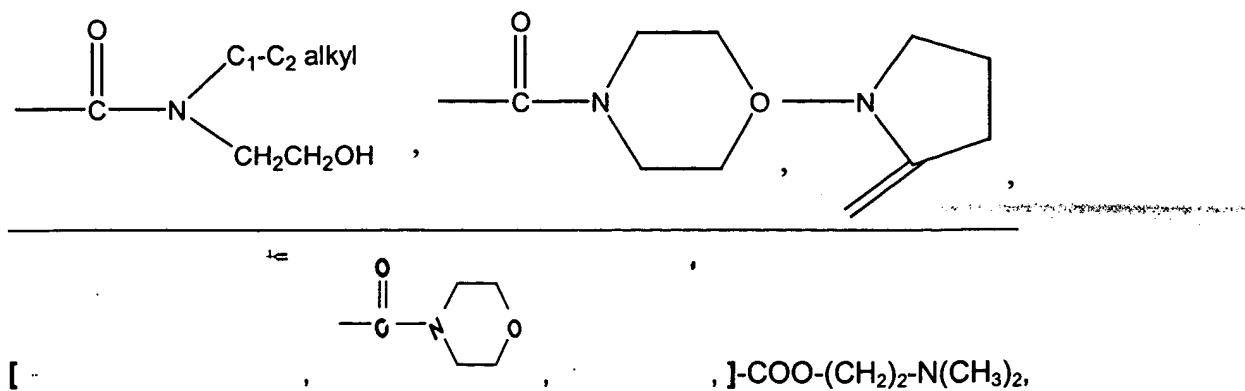


[(3c),]

wherein R₂ and R'₂ are each independently C₁-C₄-alkyl, An⁻ is an anion, v is an integer from 2 to 250, and Q" is a monovalent group that is suitable to act as a polymerization chain-reaction terminator; or

Page 61, please amend lines 1-5 as follows:

A particularly preferred group of non-ionic substituents of B or B' comprises the radicals -CONH₂, -CON(CH₃)₂, -CONH-(CH₂)₂-OH,

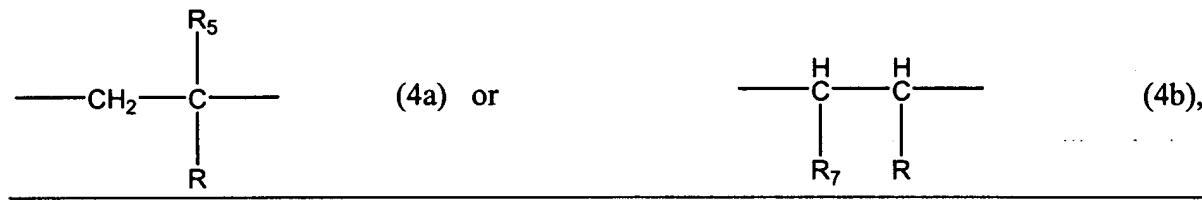


and $-\text{COO}(\text{CH}_2)_{2-4}\text{-NHC(O)-O-G}$ wherein $-\text{O-G}$ is the radical of trehalose.

(ii) anionic substituents:

Page 64, please amend lines 14-22 as follows:

B denotes for example a radical of formula



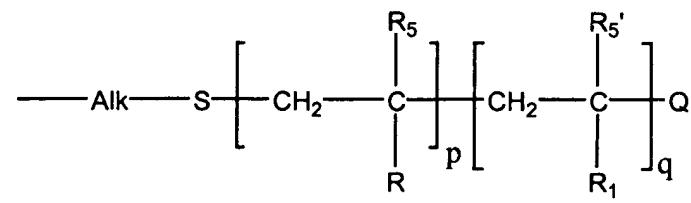
[(4a) or

(4b),]

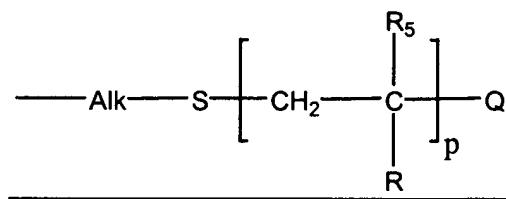
wherein R_5 is hydrogen or $C_1\text{-}C_4$ -alkyl, preferably hydrogen or methyl; R_6 is a hydrophilic substituent, wherein the above given meanings and preferences apply; R_7 is $C_1\text{-}C_4$ -alkyl, phenyl or a radical $-\text{C}(\text{O})\text{OY}_9$, wherein Y_9 is hydrogen or unsubstituted or hydroxy-substituted $C_1\text{-}C_4$ -alkyl; and R_8 is a radical $-\text{C}(\text{O})Y_9'$ or $-\text{CH}_2\text{-C}(\text{O})\text{OY}_9'$ wherein Y_9' independently has the meaning of Y_9 .

Page 65, please amend lines 11-23 as follows:

If (oligomer) is a telomer radical of formula (3a), the radical -(alk)-S-[B]_p-[B']_q-Q preferably denotes a radical of formula



(3a') and even more preferably of the formula

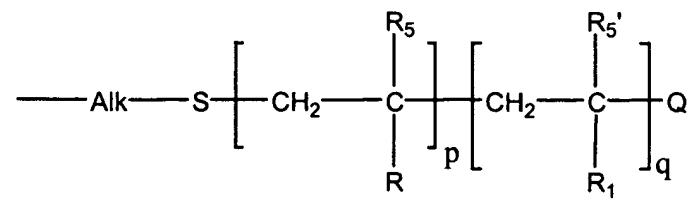


(3a'')

wherein for R₅, R₆, Q, p and q the above-given meanings and preferences apply, for R_{5'} independently the meanings and preferences given before for R₅ apply, and for R_{6'} independently the meanings and preferences given before for R₆ apply or R_{6'} is a hydrophobic substituent selected from the group consisting of hydrogen, -CN, C₁-C₁₈-alkanoyl, C₁-C₁₆-alkyl, C₁-C₁₆-haloalkyl, phenyl, C₁-C₆-alkylphenyl, C₂-C₁₀-perfluoroalkyloxycarbonyl or a corresponding partially fluorinated alkyloxycarbonyl

Page 66, please amend lines 10-22 as follows:

benzylene, (alk*) is C₂-C₄-alkylene, and (oligomer) denotes a radical of formula

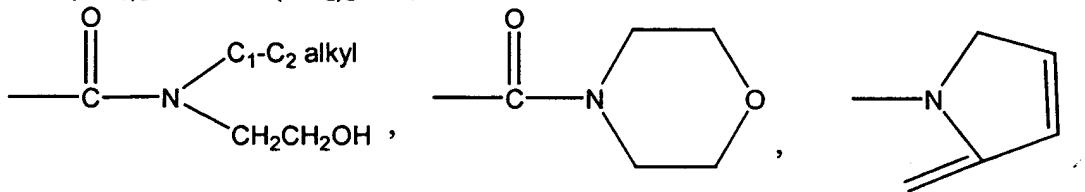


(3a'),

wherein (alk) is C₂-C₆-alkylene, Q is a monovalent group that is suitable to act as a polymerization chain-reaction terminator, p and q are each an

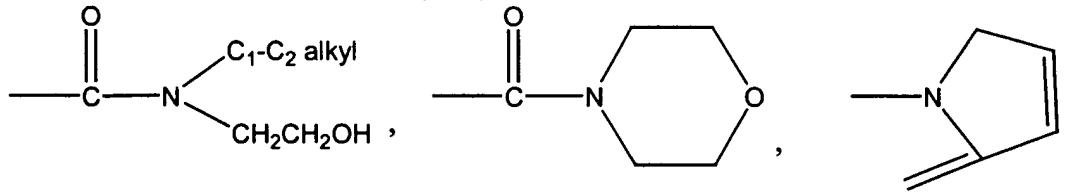
integer of from 0 to 100 and the total of (p+q) is from 5 to 100, R₅ and R_{5'} are each independently of the other hydrogen or methyl, and for R₆ and R_{6'} each independently of the other the meanings and preferences given before apply. One particularly preferred embodiment of the above outlined hydrophilic macromers comprises those wherein q is 0, p is from 5 to 100, R₅ is hydrogen or methyl, and R₆ is a radical -CONH₂, -

CON(CH₃)₂, -CONH-(CH₂)₂-OH,



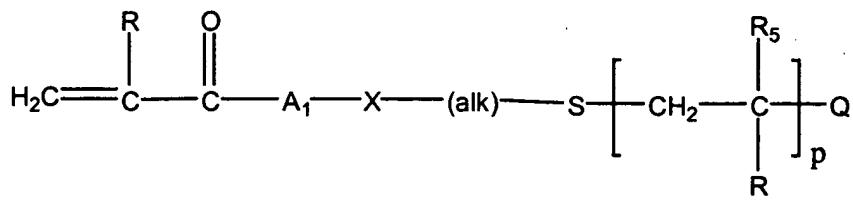
Page 67, please amend the page as follows:

[] -COO-(CH₂)₂-N(CH₃)₂, or -COO(CH₂)₂₋₄-NHC(O)-O-G wherein -O-G is the radical of trehalose. A further preferred embodiment of the above outlined hydrophilic macromers comprises those wherein p is from 4 to 99, q is from 1 to 96 wherein in the total of (p+q) is from 5 to 100, R₅ and R_{5'} are each independently hydrogen or methyl, R₆ is a radical -CONH₂, -CON(CH₃)₂, -CONH-(CH₂)₂-OH,



[] -COO-(CH₂)₂-N(CH₃)₂, or -COO(CH₂)₂₋₄-NHC(O)-O-G wherein -O-G is the radical of trehalose, and R_{6'} independently has the meaning of R₆ or is carboxy, subject to the proviso that R₆ and R_{6'} are different.

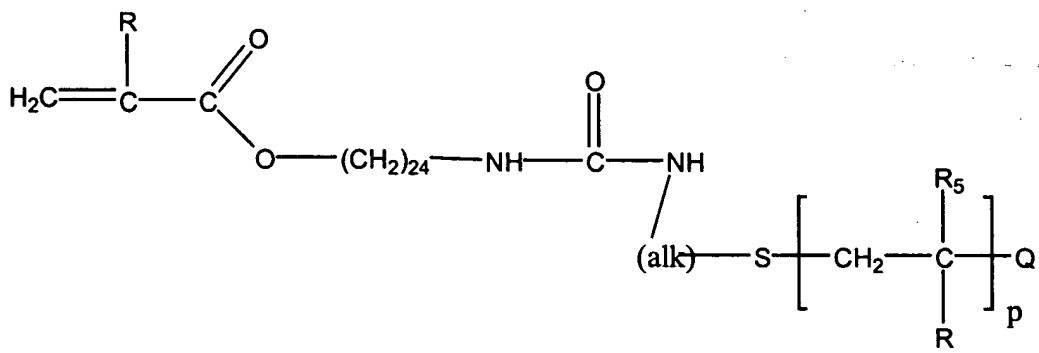
A more preferred group of suitable hydrophilic macromonomers according to the invention comprises compounds of formula



(1a),
 wherein R is hydrogen or methyl, A₁ is -O-(CH₂)₂₋₄-, -O-CH₂-CH(OH)-CH₂- or a radical -O-(CH₂)₂₋₄-NH-C(O)-, X is -O- or -NH-, (alk) is C₂-C₄-alkylene, Q is a monovalent group that is suitable to act as a polymerization chain-reaction terminator, p is an integer from 5 to 50, R₅ is hydrogen or methyl, and for R₆ the above given meanings and preferences apply.

Page 68, please amend lines 1-10 as follows:

A particularly preferred embodiment of the invention relates to hydrophilic macromonomers of the formula



(1b),
wherein for R, R₅, R₆, Q, (alk) and p the above-given meanings and preferences apply. A particularly preferred group of hydrophilic macromonomers are compounds of the above formula (1b) wherein R is hydrogen or methyl, (alk) is C₂-C₄-alkylene, R₅ is hydrogen or methyl, p is an integer of 5 to 50, Q is as defined before, and for R₆ the above given meanings and preferences apply.

In the claims:

Please amend claims 1, 2, and 4-11 as follows:

1. (Amended) A method for modifying the surface of an article, said method comprising the steps of:

a) depositing at least a [partially functionalized] polyelectrolytic tie layer onto the surface of said article, wherein said polyelectrolytic tie layer is composed of (i) one layer of a first polyionic material which is not covalently attached to the surface of the article or (ii) at least one layer of the first polyionic material which is not covalently attached to the surface of the article and at least one layer of a second polyionic material having charges opposite of the charges of the first polyionic material, wherein said first and second polyionic materials have functional groups which provide [so as to create a surface having] reactive sites for the further attachment of various active agents to the surface of the article; and

b) [chemically attaching] grafting a layer of an active agent to said reactive sites.

2. (Amended) The method of claim 1 wherein said [chemical attaching] grafting step is effected by a method chosen from the group consisting of precipitation reactions, covalent reactions, hydrogen bonding, and polymerization reactions.

4. (Amended) The method of claim 1 wherein in the step of depositing two or more [said] polyelectrolytic tie layers [is] are successively deposited onto said article surface [by applying successive electrolytic tie layers].

5. (Amended) The method of claim 1 wherein in the step of depositing one [said] polyelectrolytic tie layer is deposited onto said article surface [by a single coating application].

6. (Amended) The method of claim 1 wherein said polyelectrolytic tie layer is deposited onto said article surface by [dipping] contacting said article with one or more polyionic material solutions.

7. (Amended) The method of claim 6 wherein said layer is deposited by dipping said article into a first solution comprising [a] the first polyionic [moiety] material having [a] positive or [a] negative charges, removing said article from said first solution, dipping said article into a second solution comprising [a] the second polyionic [moiety] material having [a] charges that [is] are opposite [from said first solution] of the charges of the first polyionic material, and removing said article from said second solution.

8. (Amended) The method of claim 6 wherein said polyelectrolytic tie layer is deposited onto said article surface by dipping said article into a solution comprising [polyionic moieties of different charges] the first polyionic material and the second polyionic material and then removing said article from said solution.

9. (Amended) The method of claim [1]6 wherein [said polyelectrolytic tie layer is deposited onto said article surface by spraying] said contacting occurs by spraying a solution onto the medical device.

10. (Amended) The method of claim 9 wherein said polyelectrolytic tie layer is deposited by spraying said article with a first solution comprising the first polyionic material having positive or negative charges [a polyionic moiety having a positive or a negative charge] and then spraying said article with a second solution comprising the second polyionic material having charges opposite of the charges of the first polyionic material [a polyionic moiety having a charge that is opposite from said first solution].

11. (Amended) The method of claim 9 wherein said polyelectrolytic tie layer is deposited onto said article surface by spraying said article with a solution comprising the first polyionic material and the second polyionic material [polyionic moieties of different charges].